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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,423	02/08/2002	Minutza Leibovici	1662/51303	1722

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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 06/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,423	LEIBOVICI ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,9-18,20-28,30,32-35,39 and 43-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 9-18, 20-28, 30, 32-35, 39, and 43-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Amendments/Arguments received on April 12, 2005 is acknowledged. Claims **1-6, 9-18, 20-28, 30, 32-35, 39, and 43-51** are pending in this application.

Rejections Withdrawn

The rejection of claims 6-9 and 11-15 under 35 U.S.C. 102(a) as being anticipated by Dreckmann-Behrendt (5914336) is withdrawn in view of the amendments made 4/12/05.

The rejection of claims 2-9, 11, 13-15 under 35 U.S.C. 101 as claiming the same invention as that of claims 1-7, 9-12 of prior U.S. Patent No. 6,482,417 is withdrawn in view of applicant's arguments.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 11-15, and 50-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is directed to a stable composition wherein no more than 15% of modification II rearranges into modification I upon storage for at least 3 months. However, parent claim 6 is directed to a stable composition wherein no more than 15% of modification II rearranges into modification I upon storage for at least 3 months. Thus, claim 9 does not further limit the parent claim and the intended limitation is unclear.

Claim 12 is directed to a stable composition of claim 11 wherein the torsemide modification II comprises about 0.5-2% of torsemide modification I. However, claim 11 recites wherein the torsemide modification II contains trace amounts of about 0.5-2% of modification I. Thus, claim 12 does not further limit the parent claim and the intended limitation is unclear. It appears applicant is claiming a composition with torsemide modification I at trace amounts. If this is the case, the examiner suggests restructuring the claims to read "The stable pharmaceutical formulation of claims 11 wherein the torsemide modification II is torsemide modification II containing torsemide modification I at trace amounts."

Claim 32 recites the limitation "the high purity" torsemide modification II which lacks antecedent basis for this limitation in the claim.

Claim 50 is directed to a stable composition comprising excipients selected from lactose anhydrous NF, crospovidone NF....". The terminology NF is unclear and indefinite. Claim 51 is rejected under indefiniteness since it depends on claim 50.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16-51 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 6,482,417. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons:

Instant application claims a high purity torsemide modification II. The dependent claims recite a stable product that does not rearrange over time for at least three months. Further, the dependent claims recite particle sizes of 200, 100, and 50 microns.

US patent claims a pharmaceutical composition comprising torsemide modification that does not rearrange over time. The dependent claims recite a stable product that does not rearrange over time at least for three months. Further the dependent claims recite particles sizes of 200, 100, and 50 microns.

Although, US patent is directed to a composition and instant application claims the compound, this is deemed an obvious modification since the compound in any carrier such as water or buffer would read on a composition.

Response to Arguments

Applicant states that a terminal disclaimer will be filed when the claims are found to be allowable.

The rejection is held in abeyance until the claims are allowable over the prior art.

The rejection of claim 1 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of 81-82, 85-87 U.S. Patent No. 6,465,496 is maintained. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons:

Instant application claims a process making high purity torsemide modification II comprising the following steps: (a) adding a crude torsemide modification II to a solvent mixture comprising acetonitrile and water; (b) isolating torsemide modification II, (c) suspending the torsemide modification I of step (b) in water to form a solution; (d) adjusting the solution of step (c) to a pH of about 10+0.2; (e) filtering the solution of step (d); (f) adjusting the solution of step (e) to a pH of 6.25+0.2, and (g) isolating torsemide modification II

US '496 is directed to a process for making torsemide modification II comprising the steps of: (a) suspending amorphous torsemide in water; (b) heating the suspension; and (c) isolating torsemide modification II. In claim 82, torsemide modification II is isolated by filtration followed by drying.

The instant application is obvious over US patent '496 since US patent is directed to the broad scope of making torsemide modification II and instant application that is directed to the narrow scope. Therefore, the instant claims are encompassed by the claims of US patent '496.

Response to Arguments

Applicant argues that the instant application adjusts the pH and US '496 does not.

Applicant's arguments filed 4/12/05 have been fully considered but they are not persuasive. The examiner points out that pH adjustments during a process step is an obvious skill to practitioner in the art. The rejection is maintained since the instant claims and the claims of US '496 are directed to similar and overlapping subject matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 6, 9-18, 20-28, 30, 32-35, 39, 43-49 are rejected under 35 U.S.C. 102(e) as being anticipated by Aronhime et al (6,465,496).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Aronhime et al discloses torsemide polymorphs. The reference discloses the process of preparing torsemide modification II. Note column 10, lines 10 to column 11, line 12. The new forms of torsemide are incorporated into pharmaceutically acceptable carriers and excipients known in the art. The dosage amount is about 2 to 200 mg per day and preferably 5 to 100 mg per day. See column 10, lines 46-60. The disclosure of RE 34,672 is incorporated into the disclosure of Aronhime et al. RE 34, 672 discloses the instant particles ranges on column 3, lines 10-15.

Example 9 discloses preparing torsemide modification I by placing torsemide modification II and acetonitrile:water mixture and isolating torsemide modification II. This step reads on instant limitation (a) and (b).

Example 12 discloses placing torsemide modification I in water and adjusting the pH of the solution to 10.2 +/- 0.2 with 20% NaOH. This step reads on instant limitation (c) and (d). The solution is then filtered and the pH is adjusted to a pH of 6.25 +/- 0.2. This step reads on instant

limitation (e) and (f). The precipitate is filtered washed and torsemide modification II is isolated. This step reads on instant limitation (g).

Step (g) wherein applicant recites the isolated torsemide modification II has less than about 0.5% weight percent of torsemide modification II, is inherent since the process steps of US patent '496 and instant process steps of claim 1 are the same, thus the same product as applicant is yielded absent data showing otherwise.

With regard to the high purity torsemide modification II product claims, it is the examiner's position that the instant property limitations are inherent since both the prior art and the applicant utilize the same process of making modification II and therefore both products must be the same, absent data showing otherwise. Further, since the prior art teaches the same product as the prior art, i.e. a high purity modification II, the pharmaceutical composition will also have the same properties as the instant invention.

Response to Arguments

Applicant argues that examples 9 and 12 relied upon by the examiner are not disclosed as sequential. Applicant argues that a person would not have envisioned combining the steps of examples 9 and 12 since both aims are opposite. Applicant argues claims 6-49 are not anticipated since US '496 does not anticipate the method of making the torsemide modification and thus the product is not anticipated.

Applicant's arguments filed 4/12/05 have been fully considered but they are not persuasive. Firstly, the examiner points out that the prior art explicitly teaches the process of obtaining torsemide modification I in column 7-8 and examples 9-11 and example 9 anticipates steps (a) and (b). Example 12 discloses steps (c)-(g) wherein the starting material to obtain

modification II is torsemide modification I. See line 10 of example 12. Although the prior art does not explicitly state that examples 9 and 12 are sequential, this is an implicit disclosure since clearly one needs torsemide modification I as derived from the previous examples for the process of isolating purified modification II.

Secondly with regard to applicant's assertion that combining example 9 and 12 are equivalent to a circular route, the examiner points out that the process yields a highly purified substance. The examiner also points to the instant specification, specifically example 5, wherein the applicant also uses two *different* steps, akin to examples 9 and 12 respectively, to provide for the high purity torsemide. The examiner points out that page 20 of the specification involves the process of making the torsemide modification I by adding torsemide (modification II containing less than 20% of modification I) to a solvent mixture of acetonitrile: water to isolate torsemide modification I. This is process is the same process disclosed by the prior art in example 9. Page 21 of the instant specification discloses the second and separate process of adding torsemide modification I in water and adjusting the pH of the solution to 10.2 +/- 0.2 with 20% NaOH. The solution is then filtered and the pH is adjusted to a pH of 6.25 +/- 0.2. The precipitate is filtered washed and torsemide modification II is isolated. This process is the same process disclosed by the prior art in example 12. The examiner points out that examples 9 and 12 correspond to the **same process** disclosed in the specification step 1 and 2 respectively. Therefore, it is clear that that isolation of modification I is needed for the process of isolating modification II.

With regard to the torsemide product claims 16-18, 20-28, 30, 32 -35, 43-49 and the pharmaceutical composition claims 6 and 9-15, it is the examiner's position that since the prior art discloses the same process of making the torsemide modification II the properties, i.e. high

purity and stable upon storage and stress conditions, of the product and the composition comprising the product will be inherent in the prior art.

Accordingly it is the examiner's position that the claims are anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 2-5 under 35 U.S.C. 103(a) as being unpatentable over Dreckmann-Behrendt cited above, by itself or in view of Ortyl et al (5738872) is maintained.

As set forth above, Dreckmann-Behrendt teach the instant compound in a pharmaceutical composition. The reference teaches the use of excipients such as sugars, cellulose, and lubricating agents, known in the art, for an instant release oral tablet. Further, Dreckmann-Behrendt teaches the particle size of torsemide. (Note col. 3, lines 43-58). The reference teaches different doses (2.5 mg to 200 mg) according to dosage form and the use of torsemide as a diuretic and treatment of edema (col. 4, lines 35-60).

Dreckmann-Behrendt does not teach instant excipients.

Ortyl et al disclose that inert ingredients such as diluents (lactose), binders (povidone and cellulose), disintegrants (crospovidone), and lubricants (magnesium stearate), are known in the art of pharmaceuticals and can be used singly or in various combinations (col. 13, lines 15-45).

It would have been obvious to one of ordinary skill in the art at the time the invention was made combine the teachings of Dreckmann-Behrendt and Ortyl et al and utilize the instant excipients. One would have been motivated to do so since Ortyl et al demonstrate the state of the art in which the instant excipients are not only known to those skilled in the art but are also routinely used in the pharmaceutical art. Therefore, it is prima facie obvious to utilize conventional excipients in the pharmaceutical art to formulate a pharmaceutical composition.

Response to Arguments

Applicant argues that neither Dreckmann-Behrendt nor Ortyl et al teach or suggest a pharmaceutically acceptable excipient in a stable pharmaceutical formulation comprising an effective amount of torsemide modification 11, wherein the excipient has a low moisture content.

Applicant's arguments filed 4/12/05 have been fully considered but they are not persuasive. Firstly, the examiner points out that Ortyl teaches the instantly claimed excipients are known and utilized in the art and Dreckmann-Behrendt teaches the use of conventional excipients to formulate the pharmaceutical composition. The examiner points out that the examiner's motivation (the instant excipients are routinely utilized in the art) to combine references need not be applicant's motivation (use of low moisture excipients). Secondly, instantly rejected claims are broadly directed to a pharmaceutical composition comprising modification II and do not require **high purity** torsemide modification II. Lastly, with regard to the term "stable", the examiner points out that if the composition is capable of being stable even for 1 minute, then it reads on "a stable composition". As acknowledged by applicant torsemide modification II rearranges **over time**; thus when the composition is made, it is stable.

Accordingly, the rejection is maintained.

Conclusion

All the claims remain rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
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